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RESPIRATORY AND RIGHT HEART FUNCTION IN DIFFERENT TYPES OF OBESE PATIENTS

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16. Abstract: Eighty seven parameters of respiratory and right heart function, obtained either by direct measurement or by calculation, were measured in 63 obese patients and in a group of 17 non-obese bronchitics, the latter being used for comparative purposes. The obese patients were divided into groups according to the presence or absence of sleep disorders, the presence or absence of alveolar hypoventilation or the presence of chronic bronchitis. Twenty-nine of the parameters studied showed statistical and physiologically significant differences between the groups of obese patients, permitting the definition of a physiopathological profile for each one. This profile was characterized by specific elements relating to ventilation, gas exchange, ventilation/perfusion distribution and right-sided cardio-circulatory function. These pathophysiological "labels", particular to each type of obesity, were largely determined by the presence and dominant action of the mechanism of thoracic mechanics peculiar to each. The examination of the cyle of ventilatory regulation in the light of these findings has thrown light on the place of reflex hyperventilation, alveolar hypoventilation, the relationship between these two, and their determinant factors in each of the defined groups. The importance in obesity of ventilatory and mechanical problems, gas exchange and ventilation/perfusion distribution, as well as of right-sided cardiac haemodynamics, are also discussed in the light of the findings.

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RESPIRATORY AND RIGHT HEART FUNCTION IN DIFFERENT TYPES OF OBESE PATIENTS *

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INTRODUCTION

The role of obesity on the respiratory and cardiac functions has been the object of a great number of studies since the /916**** description and characterization of the Pickwickian syndrome by Burwell in 1956. In 1959, Auchinchloss and Gilbert published a review of observations on obesity with alveolar hypoventilation, previously reported by Kerr and Lagen in 1936. However, the difference between clinical and physiological situations, and the results sometimes contradictory of the analysis of these observations, make the comparison very difficult. In general, Pickwickian obesity, in which the patient presents an increase in weight but also diurnal hypersomnolence and respiratory apnea during sleep, has been studied with more details. Often the authors have accentuated some aspects of the physio-pathological picture to which they gave an important role, either in the genesis of

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the abnormalities observed, or in the consequences particular to obesity.

The changes in the peripheral respiratory function and alveolar hypoventilation have been shown to be most important by Fishman (1957), Bedell (1958), Benedetti (1958), Coates (1958), Alexander (1959), Cullen (1962), while for Weill (1957) and Smith (1959) the polycythemia was the most interesting fact. The right heart function was the main focus for Counihan (1956), Smith (1956), Sieker (1955), Deide (1957), Gotzche (1957), Broustet (1959) and Alexander (1962), while others such as Johnson (1956), Lillington (1957), Berlyne (1958), Perret (1959), Billiet (1960), Justin-Besancon (1962) gave an equal attention to respiratory and right sided cardiac functions.

In 1964, Billiet, Van de Woestijne and Gyselen compiled an important review on the repercussion of obesity on physiological indices available in cardiorespiratory exploration. However, one can wonder if the cardiorespiratory abnormalities described are present in all cases of obesity or only in Pickwickian obesity cases; if the latter have an exaggeration of physiological changes present in all obese patients, or if they have particular characteristics. Obese patients represent 6% of the cases examined by respiratory function specialists.

In this work an attempt is made to define the effects of obesity on the main parameters of respiratory and right heart function in 63 obese patients, included in a group of 80 cases. For comparative purposes, and in order to analyze only cases absolutely comparable for other clinical and functional dysfunctions, the patients were divided into three distinct groups on the basis of two clinical criteria: (1) the presence

or absence of hypersomnia, with central nervous disorder causing respiratory apnea (dysfunction of the respiratory center) and (2) the presence of well characterized chronic bronchitis. /917

Hypersomnia patients were then divided into two groups: those with alveolar hypoventilation and the others. A statistical analysis was performed, within and between the groups of patients, of the respiratory and cardiac functions parameters. This analysis should reveal the role, dominant or not, of obesity on the parameters considered, either in a uniform manner for all types of obesity or as a general characteristic of one or the other type of obesity.

MATERIALS AND METHODS

A. Groups of patients

The population consists of 80 patients, 63 of them being obese. Obesity is defined by the relationship real weight/ideal weight, the denominator obtained from the Lorentz formula, and expressed in the adult by the equation:

$$\text{ideal weight} = (\text{size cm} - 100) - \frac{\text{size cm} - 150}{4}$$

This number was greater than 140% in the 63 obese patients in a group homogeneous for other biometrical characteristics (average size 168 cm [σ= 6 cm], age 55 years [σ = 11 years]).

The 80 patients were divided into four groups:

(1) The true obese (9 cases) where obesity is the only pathological characteristic in the absence of other clinical consequences.

(2) The group of hypersomnolent obese (29 cases). These patients present also brutal and irrepressible attacks of diurnal hypersomnia with periods of various length of apnea,

which also happen during nocturnal sleep. This group was then subdivided into three categories on the basis of the consequences of the obesity of the cardiorespiratory functions.

a) A group of hypersomnolent obeses showing no other heart or respiratory clinical signs (12 cases).

b) A group of obese hypersomnolents with alveolar hypoventilation and right heart insufficiency (12 cases).

c) A group of obese hypersomnolents treated because they presented signs of alveolar hypoventilation and right heart insufficiency (5 cases).

(3) A group of obese cases associated with chronic bronchitis. (25 cases)

(4) The group of non-obese chronic bronchitic patients (17 cases) studied for comparative purposes, to try to dissociate the effects on chronic bronchitis from those of obesity on the function, and to determine a possible additive effect.

In those 80 patients examined outside of an acute respiratory crisis, we have compared 87 physiological elmments such as biometrics, ventilation, gas exchange, perfusion distribution and haemodynamics (E. Benignus, 1970). Normal values used for standard were obtained from the CECA tables minus 2 σ for the subjects of the same age and size.

The numerical values of these parameters were submitted to statistical analysis by calculation of the mean values, standard deviation and confidence interval (P). In order to compare the group, a t test of Student-Fisher with a probability of 0.05 was applied to each group and to each parameter. /918

B. Measurements

The normal methods used in the exploration of the respiratory function were applied.

(1) Spirography realized in an upright position with a ventilated spirograph in closed circuit (Knipping 210D apparatus and Magnatest). The residual volume is measured by the method of helium dilution in closed circuit.

(2) Analysis of blood gases. The arterial blood is collected anaerobically from the humoral artery with a trocar of Cournand, and the venous blood mixed in the pulmonary artery across a microcatheter. The results of the sample analysis are read directly on a radiometer including a Clark electrode for O_2, a Severinghaus electrode for CO_2 and an Astrup electrode for pH determination. All estimations are made in duplicates. Samples are taken with the patient at rest, after 2 minutes of directed hyperventilation, and at the fifth minute of a 40 watts effort in laying down position (vO_2 = 800 to 1,000 ml.) The determination of the concentration of O_2 and CO_2 mixed in the arterial and venous blood allows calculations of the cardiac output and of the shunt output Q_s, as well as the ratio of total venous input by the classical equation (Q_s/Q).

(3) Distribution. Analysis of the partial pressure of expired gas is carried out in parallel with the analysis of a very small amount of exhaled air obtained from the mouth, by mass spectrometry with an SM100 R (CSF) and by a pneumoradiography with volume integration. Determination of the mean alveolar

pressure permits the estimation of alveolo-arterial pressures, and the determination of the absolute and relative values of the alveolar and physiological dead spaces.

(4) A rest of inspiration by the Fowler technique is performed in dorsal decubitus and then in upright position. The variation in the concentration of exhaled nitrogen is measured between 750 and 1,250 ml of exhaled volume.

RESULTS

Of the 87 parameters originally measured for each of the 80 patients, 30 were obtained by direct measure and the others by calculations from equations classical in respiratory physiology (Benignus, 1970). Forty-six of the indices show significant statistical differences, but we will consider only the 29 variables which are concomitant in their physiological meaning, and which best represent the total functional elements such as ventilation, gas exchange, ventilation/perfusion distribution and right sided cardiac haemodynamics.

For each of the four defined groups of patients, we will establish a profile characteristic of their functions of ventilation, gas exchange, distribution and right heart functions. These data are presented in the four tables (I to IV). /919

TABLE I

FUNCTIONAL HISTORY OF THE TRUE OBESE PATIENTS

FUNCTIONAL RESULTS IN THE GROUP OF OBESE PATIENTS

Ventilation Data

CV mes.	3794**	ml
CI	79	%
VRI	2555**	ml
VRE	794	ml
Vt	455	ml
fr	17	
VR	1308	ml
VR/CT	-2	%
Vt/CRF	21	%
VEMS mes.	2827**	ml
VMM mes.	78*	l/min

Gas exchange Data

	At rest	Under stress
pH	7,41	7,39
PaO_2 mmHg	79	86
$PaCO_2$ mmHg	34	36*
$CaCO_2$ vol %	45*	47
pH $\bar{V}$	7,38	7,32
$C\bar{V}CO_2$ vol %	48**	53*

Forced Hyperventilation

PaO_2	111** mmHg
$PaCO_2$	24** mmHg
ΔPaO_2 (H-R)	33 mmHg

Distribution and Haemodynamics Data

	At rest	Under stress
VD/Vt %	41	35*
$VDalv/Vt$ %	7	12
$P(a-A)CO_2$ mmHg	4,8	6,5
$\dot{Q}s/\dot{Q}$ %	15	6,1*
Cardiac Index l/min/m²	2,9	4,8
PAP mmHg	17	27*

$\dot{V}A/\dot{V}$ %	64*
Hematocrit	48 %

* $p < 0,05$

** $p < 0,01$

n = 9 cases

The respiratory function is only slightly different from the normal patients of the same age and size. The physiological profile is characterized by:

At rest

1) Mild respiratory insufficiency without bronchial obstruction.

2) Preservation of the best inspiratory capacity in all groups of obese patients (better VRI).

3) A state of chronic gaseous alkalosis pointing to a permanent reflex hyperventilation, consequently of a stimulus for hypoxemia.

4) A correct purification of the zone of gaseous exchange (Va/V = 64%).

5) A good storage of hematosis as detected by the test of voluntary hyperventilation.

6) A moderate variation in the ventilation/perfusion distributions. This raises the physiological dead space, mainly by the presence of alveolar dead space, which, added to an equality in the P(a-A) CO_2 reveals a defect in the circulatory distribution. The distribution inequalities cause a venous input Q_s/Q triple the normal value, and are at the origin of the hypoxemia.

7) An absence of pulmonary artery hypertension (HTAP) but a drop in the cardiac index.

Under stress

1) An improvement of gas exchange bound to a standardization of the ventilatory distribution which brings the venous input Qs/Q back to normal value.

2) Slight increase in the inequality of circulatory distribution.

3) Cardiac index stays lowered and a mild stress HTAP appears.

TABLE II

FUNCTIONAL RESULTS IN OBESE PATIENTS WITH HYPERSOMNIA

A = Without hypercapnia | B = With hypercapnia | C = Treated for Hypercapnia

Ventilation Data				Gas exchange Data							Distribution and Haemodynamics Data						
					At rest			Under stress				At rest			Under stress		
	A	B	C		A	B	C	A	B	C		A	B	C	A	B	C
CV ml	3520**	2710	2830	pH	7,41	7,35**	7,39	7,39	7,35*	7,35	$\dot{V}D/Vt$ %	Insufficient strength	47	45	Insufficient strength	48	Insufficient strength
Ct %	80	73	74	PaO_2 mmHg	60	66	74	87*	73	75	$\dot{V}Daly/\dot{V}t$ %		8	4		6*	
VRI ml	2379**	1702	1665	$PaCO_2$ mmHg	36	49**	38	36*	47	40	$Pa-A\bar{C}O_2$ mmHg		4,8	3,2		4,8	
VRE ml	710	664	760	$CaCO_2$ vol %		54			45		$\dot{Q}s/\dot{Q}$ %		27	16		37*	
Vt ml	442	340*	458	pH v		7,20**	7,35		7,29		Cardiac index		2,8	4,3		8,2	
fr	20	23*	20	$C\bar{V}CO_2$ vol %		58			60		$\bar{P}AP$ mmHg		26	21		37	
VR ml	1308	1604	1322	Forced hyperventilation													
VR_{CT} %	N	N	-3	PaO_2	112**	97	102	mmHg			%		2,9	← décubitus dorsal			
$Vt/_{CRF}$ %	21	14*	23	$PaCO_2$	24**	35	28	mmHg			ΔN_2		12,1	← Upright			
VEMS mes. ml	2754**	1691	2000	ΔPaO_2	32	30	28	(H-R) mmHg									
VMM mes. l/mn	85*	55	49	$\dot{V}A/\dot{V}$		48	61	%									
				Hte	46	58*	49	%									

* $p < 0,05$

** $p < 0,01$

n = 29 cases

A – OBESE HYPERSOMNELENTS SHOWING NO CLINICAL CARDIORESPIRATORY SIGNS

The table is identical to the table for the truly obese but with the respiratory performance figures slightly lowered. But none of the physiological parameters studied allows a distinction between those two groups.

B – OBESE HYPERSOMNOLENTS WITH ALVEOLAR HYPERVENTILATION AND RIGHT HEART INSUFFICIENCY.

By definition, their cardiopulmonary function is more damaged in spite of a weight comparable to that of the true

obese patient, and even lower than in the others of obese hypersomnolents. But they also show some particular characteristics.

At rest /921

1) A restrictive respiratory insufficiency is more evident than in the other obese patients, with an obstructive component. Their thorax is smaller and less expansible, and the ventilatory reserve inferior (CV and VMM lowered).

2) There is a total and definite respiratory insufficiency with homogenous alveolar hypoventilation. This fact seems to be explained by an inefficient use of the dead space. The respiratory frequency is characteristically the greatest; on the contrary, their constant volume and the ratio V_t/CRF are the lowest of all the obese patients groups: perfect condition for a uniform total alveolar hypoventilation.

3) The inequalities in the ventilation/perfusion distribution are identical to that of the true obese patient. They are moderate, with a circulatory element [Vd\ alveolar, P(a-A) CO_2], indirectly confirming the homogeneous\characteristic of hypoventilation.

4) The venous input Qs/Q is almost five times greater than normal, expressing a decrease in the filtering in the zone of gas exchange (Va/V = 48%). /922

5) A strong increase of the ventilatory asynchronism in upright position relative to a dorsal decubitus when the Fowler test becomes only slightly pathological.

6) Absences of the reflex hyperventilation seen in all the other groups of obese, true or hypersomnolent, though they have a comparable hematosis storage during voluntary hyperventilation.

7) A characteristic polycythemia, even though the non-obese bronchitis patients do not present it with a similar arterial hypoxemia.

8) The most important decrease in the cardiac index and by definition a HTAP.

Under stress

1) A well-marked homogeneous alveolar hypoventilation, expressed by a slight improvement in the blood gas.

2) A definite increase of the venous input Qs/Q without any change in the indices of ventilatory and circulatory distribution relative to the rest state which emphasizes a reinforcement of the homogeneous character of the hypoventilation.

C - HYPERSOMNOLENT OBESE PATIENTS AFTER TREATMENT OF THEIR ALVEOLAR HYPOVENTILATION AND OF THEIR RIGHT-SIDED HEART INSUFFICIENCY

At rest

1) Persistancy of the function of thoracic mechanics comparable to what it was before treatment. In fact, the thorax has a better expansion, but the distribution of the different volumes in the total pulmonary capacity stays the same; and the expansion is definitely weaker than in the

true obese or in the obese hypersomnolents who have never shown alveolar hypoventilation signs.

2) Preservation of a slight obstructive component, and of a good hematosis storage in hypoventilation.

3) Disappearance of the homogeneous alveolar hypoventilation without change in the ventilation/perfusion distributions. These facts agree with a slowing down of the respiratory frequency, an increase in the tidal volume, and a more standard V_t/CRF ratio which relieves the inefficiency in the use of the dead space.

4) A return to a purification almost normal of the zone of exchange (Va/V = 61%) and a venous input Qs/Q identical to the group I (true obese). /923

5) Disappearance of the polycythemia.

6) Standardization of the cardiac index, but slight residual HTAP.

Under stress

No modification of the gas exchange.

Table III — Functional results in the group of non-obese bronchitics

Their physiopathological profile is well known. Only the most important elements are described here to allow a comparison with the next group of patients associating chronic bronchitis and obesity.

TABLE III

FUNCTIONAL RESULTS IN THE GROUP OF NON-OBESE BRONCHITICS

Ventilation

Data	
CV	2640 ml
CI	63,5* %
VRI	1185 ml
VRE	1020* ml
Vt	461 ml
fr	19
VR	2732** ml
VR/CT	+19* %
Vt/CRF	13* %
VEMSmes	900* ml
VMMmes	26 l/min

Gas exchange

Data	At rest	Under stress
pH	7,40	7,37
PaO_2 mmHg	67	68
$PaCO_2$ mmHg	42	46
$CaCO_2$ vol %	50	52
pH $\bar{v}$	7,38	7,31
$C\bar{v}CO_2$ vol %	53	57

Forced hyperventilation

PaO_2	83 mmHg
$PaCO_2$	36 mmHg
ΔPaO_2 (H-R)	15* mmHg

Distribution and Haemodynamics

Data	At rest	Under stress
V_D/V_t %	49	43
$\dot{V}Dalv/\dot{V}t$ %	16**	12
P(a-A)CO_2 mmHg	12**	10*
$\dot{Q}s/\dot{Q}$ %	24	18
Card. index l/min/m²	3,6	6,4
PAP mmHg	20	36

ΔN_2 % décubitus dorsal 10,7 / Upright

$\dot{V}A/\dot{V}$ 47 %

Hématocrite 44 %

* $p < 0,05$
** $p < 0,01$
n = 17 cases

At rest

1) Ventilatory insufficiency of both obstructive and distensible character. The increase in the VR and in the ratio VR/CT is an obvious sign of pulmonary distension, but so is /924 the permanence of the forced inspiratory posture of the thoracic cage, which expresses itself by a decrease in the inspiratory capacity. However, compared to the obese, the bronchitic keeps a normal VRE.

2) The respiratory insufficiency is also total but the alveolar hypoventilation is heterogeneous and distributive. The respiratory frequency and the tidal volume are normal. Only the ratio V_t/CRF is decreased as in the hypersomnolent obese group with alveolar hypoventilation.

3) The decrease of the efficiency of purification in the zone of exchange is comparable to the same decrease in the obese hypersomnolent patients in hypoventilation (Va/V = 47%). However, a physiological V_d greater, and a greater inequality in circulatory distribution emphasizes the character more heterogeneous of hypoventilation. The venous input Qs/Q is four times the normal value.

4) The hematosis storage is characteristically decreased.

5) The ventilation asynchronism in horizontal posture is well marked (Fowler test).

6) Absence of polycythemia reaction to the arterial hypoxemia similar in the hypersomnolent obese.

Under stress

1) Tendency to diminish the inhomogeneity in alveolar hypoventilation. This is demonstrated by a slight accentuation in hypercapnia without increase of hypoxemia and a decrease in the inequalities of the circulatory distribution (alveolar V_d and P(a-A) CO_2 lower than normal).

2) Increase of HTAP relative to the rest state.

Table IV — Functional results for the group of genuine obese patients and chronic bronchitics.

Their physiopathological profile is similar to a bronchitic and the characteristics particular to obesity are few.

TABLE IV

FUNCTIONAL RESULTS IN OBESE BRONCHITICS

Ventilation		Gas exchange			Distribution and Haemodynamics		
Data		Data			Data		
			At rest	Under stress		At rest	Under stress
CVmes	2900 ml	pH	7,39	7,36	V_D/V_t %	49	47
CI	71 %	PaO_2 mmHg	63	68	V_{Dalv}/V_t %	18**	18
VRI	1580 ml	$PaCO_2$ mmHg	44	46	$P(a-A)CO_2$ mmHg	12**	14*
VRE	813 ml	$CaCO_2$ vol %	51	53	$\dot{Q}s/\dot{Q}$ %	31	20
Vt	497 ml	pH $\bar{v}$	7,36	7,29	Card. index l/mn/m²	3,2	4,6
fr	18	$C\bar{v}CO_2$ vol %	55	59	$\bar{P}AP$ mmHg	23	49
VR	2442** ml	Forced hyperventilation			ΔN_2 décubitus dorsal	6,1 %	
VR/CT	+16* %				ΔN_2 Upright	5,1 %	
Vt/CRF	15* %	PaO_2	85 mmHg		$\dot{V}A/\dot{V}$	51 %	
VEMS mes	1300 ml	$PaCO_2$	36 mmHg		Hématocrit	53 %	
VMM mes	41 l/min	$\Delta Pa\,O_2$ (H-R)	21 mmHg		* $p < 0.05$ ** $p < 0.01$ n = 25 cases		

At rest

1) The ventilatory insufficiency is mixed, distensive /925 and the bronchial obstruction is a dominant trait.

2) The respiratory insufficiency is total and the alveolar hypoventilation is heterogeneous. Respiratory frequency and tidal volume are normal, and only the V_t/CRF ratio is significantly lowered.

3) The loss of efficiency of purification in the zone of exchange is concomitant to inequalities of distribution very similar to the ones in the non-obese bronchitics. Venous input is five times the normal value.

4) The hematosis storage determined in voluntary hyperventilation is of the bronchitic type.

5) Presence of definite ventilatory asynchronism by the Fowler test.

6) A modification of the right-sided haemodynamics higher than in the obese bronchitics (HTAP and decrease of the cardiac index).

7) Three characteristics particular to obesity persist: polycythemia, no distension of the thoracic cage at rest (inspiratory capacity almost normal); distension occurs exclusively by the VR; improvement of the ventilatory distribution in upright posture (Fowler test). /926

Under stress

1) As for the bronchitics, tendency to an increase in homogeneity of alveolar hypoventilation, and to fixed distribution inequalities.

2) A greater strength of the pulmonary vessels than in the non-obese bronchitics. Under the same conditions of stress, the obese bronchitics display the highest HTAP of all the groups of patients in the study.

DISCUSSION

We cannot elaborate on all the questions raised by the study of 29 respiratory and cardiovascular indices having one or several times a statistical significance characteristic of one or the other of the type of obesity defined or of the obesity in general. But we would like to keep a discriminative value to our results, since the samples chosen are absolutely comparable from a biometric point of view. They are very different from the monstrously obese previously chosen to study the influence of obesity on respiration. They represent a sample of obese patient more frequently examined in functional exploratory practice.

The respiratory function is always impaired relative to a normal subject of the same age and size. By increasing order of functional disorders one records: the true obese and the hypersomnolent obese without cardiorespiratory insufficiency who are comparatively incapacitated, then the hypersomnolent obese after treatment for CR insufficiency, and then the hypersomnolent obese with alveolar hypoventilation and right-sided cardiac insufficiency. For the neurologists (Escande, 1967) those form the group of Pickwickian obese of the "Burwell" type, and the obese hypersomnolent without alveolar hypoventilation represent the group of Pickwickian type "Joe".

A. The ventilatory parameters

Obesity, of the Pickwickian type or not, decreases the ventilatory capacity of the thoracic cage. We found in all types of obesity without bronchitis a decrease in CPT, CV, VRE, VEMS, described long ago by numerous authors: Sieker (1955),

Caroll (1956), Bedell (1958), Benedetti (1958), Hackney (1959), /927
Cullen (1962), Billiet (1964), and Brune (1967). But the decrease in CPT is not distinctive in itself of obesity since a similar decrease is observed in the chronic bronchitics. The classical elective decrease in VRE is less significant of obesity than an increase in VRI. Confirming the results of Brune (1967), we observed a slight decrease in VR in the true obese, but not an increase in the Pickwickian obese as described by Gamain (1965). It is very likely that the patients of this researcher had also chronic bronchitis. Our results demonstrate that the "Burwell" type of Pickwickians is characterized by an important loss of the thoracic expansion relatively to the other types of obese, even Pickwickian type "Joe", and by the presence of an obstructive component which they are the only one to display. We could find a satisfactory explanation for this elective decrease of the thoracic expansion, in particular in the repartition of their subcutaneous lipid reserves. We did not find the specific morphological types android and gynoid described by Justin-Besancon in 1962. On the same subject, Fadell (1962) worked on the intercostal lipomatosis present in the "Burwell" Pickwickians and absent in the other types of obesity.

B. Gas Exchange

The most important point is that all the groups of obese, showing or not a well-characterized central defect by specific encephalographic exploration: apnea during their sleep or onslaughts of diurnal hypersomnia, have a normal and efficient capacity of voluntary hyperventilation. However, this capacity is induced by reflex only in the true obese and in the obese hypersomnolents of the type "Joe" with a central nervous system defect. In the Pickwickian type "Burwell" showing

clinical and encephalographic signs of a similar central deficiency, this reflex hyperventilation is completely absent, so that this group is significantly different from others in our study. This rapid sweep of the dead space by lowered tidal volume seems responsible for the unique homogeneous alveolar hypoventilation. This specific and particular modification of the function $V_t \cdot f$ is seen only in this group and disappears rapidly as well as the alveolar hypoventilation, after treatment. In a similar experimental situation Nairmack and Cherniack (1960) and Cherniak and Guenter (1961) demonstrated that the pulmonary compliance is normal in the obese but that the compliance of their thoracic cage was grossly decreased. One third of the observed increase in mechanical ventilatory work would be due to the increased elastic resistance of the cage. These same authors, after Caro (1960), /928 have shown than in increasing the resistance to elasticity of the thoracic cage by bandage, the tidal volume was diminished, and the respiratory frequency raised exactly like for the "Burwell" Pickwickians of our study. Apparently these obese patients are the only ones who, showing an increased resistance to elasticity of the thoracic cage allowing no adaption of respiratory frequency and tidal volume, still are able to maintain their alveolar ventilation to a normal level. Since Hackney (1959) could not produce alveolar hypoventilation and change in the equation $V_t \cdot f$ by bandaging the thoracic cage in non-obese normal subjects, and since the Pickwickian of the "Joe" type are not in alveolar hypoventilation, though their net weight is the highest of all the obese groups, one can wonder which specific factor distinguishes their peripheral respiratory behavior. Is it a central or a peripheral mechanical factor, or both conjointly? Certain stages of transition between no alveolar hypoventilation and permanent alveolar hypoventilation might exist, but we have not been able to observe such cases among the obese hypersomnolents followed for several years in our study. Indeed certain cases show a slight

tendency to alveolar hypoventilation by transfer from the upright to the horizontal posture, or between the awake and the sleep states. But the precise role of the obesity is not clear since our obese hypersomnolents without hypoventilation (Pickwickian "Joe") have a net weight higher than the obese hypersomnolents with hypoventilation (Pickwickian "Burwell"). However, in the latter, the alveolar hypoventilation disappears temporarily after medical treatment and the subsequent diminution in weight.

C. Distribution - Ventilation/perfusion inequalities

From this point of view, the obese are characterized by the moderate inequalities of ventilation/perfusion distribution relative to other types of respiratory insufficiency. The physiological indices significant in our study, which express the inequalities [$P(A-a)O_2$, $P(a-A)CO_2$, different dead spaces], are not much higher than normal, and very comparable in all the groups of obese. Barrera et al. (1969) also confirms this moderate increase in the alveoloarterial difference as opposed to the important venous input in obesity. Classically this is said to be inherent to the presence of pulmonary basal areas which are actively hypoventilated relative to perfusion, due to a pathological elevation of the diaphragm in the obese patients (intra-abdominal overpressure as shown by Hackney in 1959). These facts suggest that in opposition to an opinion popular since Bedell (1958) and Cullen (1962), the respiratory insufficiency in obesity /929 is only partially determined by inequalities in their distribution V/Q. These patients have all the mechanical potentials for alveolar hypoventilation as defined by Fishmann and Goldring (1966). But it appears only in the Pickwickian type "Burwell" because this latter group probably has a peculiar mechanical arrangement in their circuit of respiratory regulation, which gives rise to specific interrelations between their V_t, their

V_d and their CRF which we have shown to be statistically significant. This contrivance is not directly related to the importance of the obesity, which does not need to be enormous since in alveolar hypoventilation, the obese have a ratio of ideal weight/real weight lower than the one in the group where alveolar ventilation is closer to normal. Furthermore, Holley (1967) has shown by the technique of functional exploration by radioactivity that only the obese in which the VRE was reduced to three quarters of the normal value, had a superfusion of the lower part of the lung and hyperventilation of the apical portions. Our data confirm the weak inhomogeneity of the circulatory distribution in the obese, including when the gas exchanges are strongly affected, by little change in the values of the $P(a-A)CO_2$ and in the ratio V_d alv./V_t relatively to the normal values. This is well in agreement with the datas of Severinghaus (1957), who showed experimentally that the more reduced current volume, the smaller the alveolar dead space. An improvement in gas exchange in the obese in upright posture was a characteristic of obesity for SAid (1960) and Tucker (1960); this depends upon an increase of the VRE in upright position and a decrease in the size of the pulmonary compartment at slow rinsing. This improvement is confirmed by our studies, except in the case of the Pickwickian "Burwell" where the ventilatory asynchronism is, on the contrary, intensified (Fowler test). In the same line of thought, Tucker (1960) observes a stability of distribution V/Q in the lungs of the obese in right-sided cardiac insufficiency between upright and dorsal decubitus posture. Also Holley et al (1967) have verified that in the obese who spontaneously ventilate in the lower part of their CV, close to the residual volume, the ventilatory distribution was inversed relatively compared to normal. For those patients the ventilation was more efficient at the apex than at the base. This is probably only the case for the hypersomnolent obese with cardiorespiratory failure.

D. Right heart haemodynamics

We observe — as Billiet (1964) — a decrease in the cardiac index for all the obese, whereas Benedetti (1958) considers it as normal. This is added to an increased cardiac output and a polycythemia, one of the most constant characteristics of/ obesity, a moderate arterial hypertension (HTAP)\ was only seen in the Pickwickian type "Burwell". The strong HTAP at rest published in the literature were probably due to the examination of patients in a state of respiratory failure much more acute than/930 ours, who were all sampled outside of the crisis (Auchincloss, 1955). Alexander (1964) submits an hypothesis where the constant elevation of pressure in the left heart plays a determining role in the genesis of the cardiac insufficiency in the obese. We have not measured systematically the capillary pressure in our patients, to be able to confirm this hypothesis, but this suggestion is interesting inasmuch as in the patients examined during the phases of moderate hypoxemia and hypercapnia, these two hypertensive factors are not active. However, polygraphic recording during nocturnal sleep in Pickwickians, with continuous recording of the pulmonary arterial pressure, shows the presence of repeated hypertensive shocks sometimes impressive. They are apparently related to an increase of the perivascular component of the pulmonary blood pressure (mechanical factors).

CONCLUSION

It is not the ambition of this work to answer all the questions brought about by the effects of obesity on the cardio-respiratory function, but it has thrown some light on a few particular points.

First of all, in the event of abnormal behavior of the respiratory center in the Pickwickian and of a normal functioning of this center in the other groups of obese patients, it is demonstrated that the importance of the physiological disorders in these patients is directly bound neither to the presence or absence of the weight overload, nor to the eventuality of a central nervous system disorder. Though it does not represent a complete determination of all the components, this work suggests that the cause of the disorder lies in the appearance, at one time or another in the obese patient's life, perhaps at the beginning, and later on related to the elective repartition of the storage of lipds, of several types of defects in the thoracic/pulmonary mechanism causing the physiopathological variations seen between the different groups of obese persons. If we start with a cause for hypoxemia by blood contamination in the pulmonary base in all of the obese, we see that, depending upon the type of obesity considered, the mechanisms possible for reflex hyperventilation are progressively reduced to the point of disappearing completely in the Burwell type of Pickwickian. In this group, the key factors in the respiratory regulation are changed so that an alveolar hypoventilation, always homogeneous, becomes necessary but stays reversible by loss of weight or medical treatment. The division of the obese in physiopathological groups is then in order; two main classes of obese patients are then defined: (1) those without /931
a possibility of voluntary hyperventilation — the bronchitic obese, and (2) all others. In this last group, by order of increasing functional disorder relative to the reduction in reflex hyperventilation, one has the true obese, the hypersomnolent obese without alveolar hypoventilation, then the hypersomnolents after treatment of their cardiorespiratory insufficiency, and last the hypersomnolent obese showing right-sided cardiac insufficiency and permanent alveolar hypoventilation. Among the hypersomnolent obese (Pickwickian), the transitory stages from one type to another remain possible, though we could not demonstrate them, suggesting that the thoracic mechanism producing alveolar

hypoventilation is particular to the Burwell type of obese. On the contrary, a transitory phase between true obesity without hypoapnea and Pickwickian obesity appears very improbable. Our results also hint that the inequalities in the ventilation/perfusion distribution in the lungs of the obese play a very minor part in the total respiratory insufficiency, but that they are the starting point for the partial respiratory insufficiency as seen in the other types of obesity. It is essentially the same for the consequences of the right-sided haemodynamics. In this group, outside of the acute phases of decompensation where the humoral factors prevail (hypoemia and hypercapnia), as in the other types of respiratory insufficiency, the thoracic mechanism and the total change in the myocardium particular to all of the obese, appear to be the deciding factors for the HTAP and CPC.

REFERENCES

1. Alexander, J. K. and E. W. Dennis. Circulatory Dynamics in Extreme Obesity. Circulation. Vol. 20, 1959, p. 662.

2. Alexander, J. K., K. Amad and W. V. Cole. Observations on Some Clinical Features of Extreme Obesity with Particular Reference to Cardiorespiratory Effects. Amer. J. Med., Vol. 32, 1962, pp. 512-524.

3. Alexander, J. K. Obesity and Cardiac Performance. Amer. J. Card., Vol. 14, No. 6, 1964, pp. 860-865.

4. Authincloss, J. H. Jr., E. Cook and A. D. Renzetti. Clinical and Physiological Aspects of a Case of Obesity, Polycythemia and Alveolar Hypoventilation. J. Clin. Invest. Vol. 34, 1955, pp. 1537-1545.

5. Auchincloss, J. H. Jr., and R. Gilbert. The Cardiorespiratory Syndrome Related to Obesity: Clinical Manifestations and Pathologic Physiology. Progr. Cardiovasc. Dis., Vol. 34, 1955, pp. 1537-1543.

6. Barrera, F., M. Reidenberg, W. L. Winters and Suwana Hungspreugs. Ventilation Perfusion Relationships in the Obese Patient. J. Appl. Physiol., Vol. 26, 1969, pp. 420-426.

7. Bedell, G. N., W. R. Wildon and P. M. Seebohm. Pulmonary Function in Obese Persons. J. Clin. Invest. Vol. 37, 1958, pp. 1049-1060.

8. Benedetti, A. and E. Zerbini. Obesity and Respiratory Function. II. Progr. med. (Napoli), Vol. 14, 1958, p. 355.

9. Benignus, E. Respiratory Physiopathology of the Pickwick Syndrome. Its Place in Obesity. Thèse Doc. Méd. No. 165, Strasbourg, 1970.

10. Berlyne, G. M. The Cardiorespiratory Syndrome of Extreme Obesity. Lancet, Vol. 2, 1958, p. 939.

11. Billiet, L, K. P. Van de Woestijne, R. Serra and A. Gyselen. Obesity and Respiratory Insufficiency. Acta. Tuberc. Pneumol. belg., Vol. 50, 1960, p. 33.

12. Billiet, L., K. P. Van de Woestijne and A. Gyselen. Obesity and Respiratory Insufficiency; In: Pulmonary Function Investigation. Médicales Flammarion, Vol. 1, 1964, 1,507 pages.

13. Broustet, P., H. Bricaud, G. Cabanieu, M. Callochio and D. Cottin. Two Cases of Chronic Pulmonary Heart Disease due to Obesity. Arch. Mal. Coeur, Vol. 52, 1959, p. 1140.

14. Brune, J. Respiratory Ailments of Obese Patients. Cahiers Med. Lyon, Vol. 43, 1967, pp. 271-285.

15. Burwell, C. S., E. D. Robin, R. D. Wholey and A. G. Bickelmann. Extreme Obesity Associated with Alveolar Hypoventilation. A Pickwickian Syndrome. Amer. J. Med. Vol. 21, 1956, pp. 811-818.

16. Caro, C., J. Butler and A. B. Dubois. Some Effects of Restriction of Chest Cage Expansion on Pulmonary Function in Man, an Experimental Study. J. Clin. Invest., Vol. 39, 1960, pp. 573-583.

17. Caroll, D. A Peculiar Type of Pulmonary Failure Associated with Obesity. Amer. J. Med., Vol. 21, 1956, pp. 819-824.

18. Cherniak, R. M. and D. A. Guenter. The Efficiency of the Respiratory Muscles in Obesity. Canad. J.Biochem. Phys., Vol. 39, 1961, pp. 1215-1222.

19. Coates, E. O., G. L. Brinkman and F. E. Noe. Hypoventilation Syndrome: Physiologic Studies in Selected Cases. Ann. Intern. Med., Vol. 48, 1958, p. 50.

20. Counihan, T. B. Heart Failure Due to Extreme Obesity. Brit. Heart J., Vol. 18, 1956, p. 425.

21. Cullen, J. H. and P. F. Formel. The Respiratory Defects in Extreme Obesity. Amer. J. Med., Vol. 32, 1962, pp. 525-531.

22. Escande, J. P., B. A. Schwartz, M. Gentilini, J. Hazard, P. Choubrac, and A. Domart. The Pickwick Syndromes. Development of Ideas. Present Concepts (according to 3 observations). Bull. soc. Méd. Hôp. Paris., Vol. 118, 1967, pp. 273-294.

23. Fadell, E. J., A. D. Richman, W. W. Ward, and J. R. Hendon. Fatty Infiltration of Respiratory Muscles in the Pickwickian Syndrome. New. Engl. J. Med., Vol. 266, 1962, pp. 861-864.

24. Fishman, A. P., J. M. Turino, and E. H. Bergofsky. The Syndrome of Alveolar Hypoventilation. Amer. J. Med., Vol. 23, 1957, pp. 333-337.

25. Fishman, A. P., R. M. Goldring and G. M. Turino. General Alveolar Hypoventilation. A Syndrome of Respiratory and Cardiac Failure in Patients with Normal Lungs. Quart. J. Med., Vol. 35, 1966, pp. 261-275.

26. Gamain, B., A. Maurel and M. Farzaneh. A Curious Respiratory Ailment. Alveolar Ventilation of Obese Patients. Pickwick Syndrome. Presse Méd., Vol. 73, No. 27, 1965, pp. 1567-1570.

27. Gotzche, H. and Petersen, Obesity Associated with Cardiopulmonary Failure; the Pickwickian Syndrome. Acta med. scand., Vol. 161, 1958, p. 383.

28. Hackney, J. D., M. G. Crane, C. C. Collier, and D. E. Griggs. Syndrome of Extreme Obesity and Hypoventilation: Studies of Etiology. Ann. Int. Med., Vol. 51, 1959, pp. 541-552.

29. Holley, H. S., J. Milic-Emili, M. R. Becklake, D. V. Bates. Regional Distribution of Pulmonary Ventilation and Perfusion in Obesity. J. Clin. Invest., Vol. 46, 1967, pp. 475-481.

30. Johnson, R. L., J. P. Lillehei and W. F. Miller. Cardiopulmonary Changes Associated with Extreme Obesity and Polycythemia. Clin. Res. Proc., Vol. 4, 1956, p. 47 (Abstr.).

31. Justin-Besancon, C., H. Lamotte, S. Lamotte-Barillon, and M. Grivaux. An Obesity Accident: Pickwick Syndrome. Evolutionary Study. Sem. Hop. Paris, Vol. 38, 1962, pp. 975-983.

32. Kerr, W. J., and J. B. Lagen. The Postural Syndrome Related to Obesity Leading to Postural Emphysema and Cardiorespiratory Failure. Ann. Intern. Med., Vol. 10, 1936, pp. 569-573.

33. Lillington, G. A., M. W. Anderson and R. O. Brandenburg. The Cardiorespiratory Syndrome of Obesity. Dis. Chest, Vol. 32, 1957, pp. 1-8.

34. Naimark, A., and R. M. Cherniack. Compliance of the Respiratory System and its Components in Health and Obesity. J. Appl. Physiol., Vol. 15, 1960, pp. 377-382.

35. Perret, Cl., and B. Baudraz. Cardiorespiratory Insufficiency Related to Obesity (Pickwick Syndrome). Schweiz. Med. Wschr., Vol. 39, 1959, p. 1289.

36. Said, S. I., Abnormalities of Pulmonary Gas Exchange in Obesity. Ann. Int. Med., Vol. 53, 1960, pp. 1121-1124.

37. Seide, M. J., Heart Failure Due to Extreme Obesity. Report of a Case With Autopsy Findings. New Engl. J. Med., Vol. 257, 1957, p. 1227.

38. Severinghaus, J. W. and M. Stupfel. Alveolar Dead Space as an Index of Distribution of Blood Flow in Pulmonary Capillaries. J. Appl Physiol., Vol. 10, 1957, pp. 335-348.

39. Siecker, H. O., E. H. Estes, Jr., G. A. Kelser, and H. D. Mc Intosch. A Cardiopulmonary Syndrome Associated With Extreme Obesity. J. Clin. Invest., Vol. 34, 1955, p. 916.

40. Smith, R. E., W. L. Hoseth, J. L. Brown, and M. E. Dempsey. Heart Failure from Hypoventilation Associated with Obesity: Report of Two Cases with Physiologic Studies. Circulation, Vol. 14, 1956, p. 1003.

41. Smith, G. M. Obesity with Polycythemia Report of a Case. Ann. intern. Med. Vol. 50, 1959, p. 1530.

42. Tucker, D. H. and H. O. Sieker. The Effect of Change in Body Position on Lung Volumes and Intrapulmonary Gas Mixing in Patients with Obesity, Heart Failure, and Emphysema. Amer. Rev. Resp. Dis., Vol. 82, 1960, pp. 782-791.

43. Weill, M. H. and A. S. Prosad. Polycythemia of Obesity: Further Studies on its Mechanism and Report of Two Additional Cases. Ann. Intern. Med., Vol. 46, 1954, pp. 60-67.

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